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Supporting Information

C–H Activation of π -Arene Ruthenium Complexes

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SUPPORTING INFORMATION

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Experimental Details

General Information

Commercially available reagents were used as received from suppliers. Solvents were laboratory grade and dried using an appropriate drying agent when required. Reactions requiring anhydrous conditions were carried out under an atmosphere of dry argon using Schlenk-line techniques. Where appropriate, solvents were sparged with argon or degassed using the freeze-thaw cycle method. Thin-layer chromatography was carried out on silica plates (Merck 5554) or neutral alumina plates (Merck Art 5550) and visualized under UV (254/365 nm) irradiation or by staining with potassium permanganate solutions. Preparative column chromatography was carried out using silica (Merck Silica Gel 60, 230400 mesh) or neutral alumina (Merck Aluminium Oxide 90, activity II-III, 70230 mesh), pre-soaked in ethyl acetate.

NMR spectra (^1H , ^{13}C , ^{19}F) were recorded on a Varian VXR-400 spectrometer (^1H at 399.97 Hz, ^{13}C at 100.57 MHz, ^{19}F at 376.5 MHz) or a Varian VNMR-700 spectrometer (^1H at 699.73 MHz, ^{13}C at 175.95 MHz). Spectra were recorded at 295 K in commercially available deuterated solvents and referenced internally to the residual solvent proton resonances.

Electrospray and high resolution mass spectrometry were performed on a Thermo-Finnigan LTQ FT system using acetonitrile as the carrier solvent

General procedure for the synthesis of $[\text{CpRu}(\eta^6\text{-arene})]\text{PF}_6$

An oven dried round bottomed flask was charged with $[\text{CpRu}(\text{NCMe})_3]\text{PF}_6$ (and arene if solid) and placed under an inert atmosphere. To this was added freshly distilled 1,2-dichloroethane (approx. 15 mL) (and freshly sparged arene if liquid). The reaction mixture was heated to reflux (90 °C) for 18 hours. The volatiles were then removed *in vacuo* to yield a powder which was dissolved in the minimum of acetonitrile or acetone and added dropwise to stirring diethyl ether to yield a colourless fine precipitate which was isolated by decanting the solution. In some cases, purification required column chromatography which was performed on silica using CH_2Cl_2 as the mobile phase.

[CpRu(η^6 -*ortho*-fluorotoluene)]PF₆

Following the *General Procedure*, [CpRu(NCMe)₃]PF₆ (112 mg, 0.258 mmol) and *ortho*-fluorotoluene (28 mg, 28 μ L, 258 mmol) were reacted to produce the *title compound* as a beige solid (88 mg, 88%); δ_{H} (Acetone-D₆): 6.79 (dd, $J = 6.0$ Hz $J = 4.5$ Hz, 1H), 6.55 (t, $J = 4.5$ Hz, 1H), 6.35 (tdd, $J = 6.0, 3.0, 1.0$ Hz, 1H), 6.20 (td, $J = 6.0, 3.0$ Hz, 1H), 5.62 (s, 5H, Cp), 2.52 (d, $J = 2.0$ Hz, 3H); δ_{C} (Acetone-D₆): 136.2 (d, $J = 274$ Hz, 1C), 93.8 (d, $J = 18$ Hz, 1C), 86.9 (d, $J = 5$ Hz, 1C), 84.5 (s, 1C), 84.1 (d, $^3J_{\text{C-F}} = 7$ Hz, 1C), 81.7 (s, 5C) 76.6 (d, $^2J_{\text{C-F}} = 23$ Hz, 1C), 14.0 (d, $^3J_{\text{C-F}} = 1$ Hz, 1C); δ_{F} (Acetone-D₆): -72.67 (d, $^1J_{\text{P-F}} = 707$ Hz), -142.2 (s, 1F); m/z (HR-ESI⁺) 270.9998 [M-PF₆]⁺ (C₁₂H₁₂F⁹⁶Ru requires 270.9999); Anal. Found (Expected): C 34.15 (34.21); H 2.87 (2.87); N 0.26 (0.00).

[CpRu(η^6 -fluorobenzene)]PF₆

Following the *General Procedure*, [CpRu(NCMe)₃]PF₆ (200 mg, 0.461 mmol) and fluorobenzene (48 mg, 47 μ L, 0.507 mmol, 1.1 equiv) were reacted to produce the *title compound* as a beige solid (153 mg, 82%); δ_{H} (Acetone-D₆): 6.82 (dd, $^3J_{\text{H-H}} = 6.0$ Hz, $^3J_{\text{H-F}} = 4.5$ Hz, 2H), 6.47 (td, $^3J_{\text{H-H}} = 6.0$ Hz, $^4J_{\text{H-F}} = 4.0$ Hz, 2H), 6.27 (td, $^3J_{\text{H-H}} = 6.0$ Hz, $^5J_{\text{H-F}} = 3.5$ Hz, 1H) 5.65 (s, 5H); δ_{C} (Acetone-D₆): 136.9 (d, $^1J_{\text{C-F}} = 276$ Hz, 1C), 85.2 (s, 1C), 84.9 (d, $^3J_{\text{C-F}} = 6$ Hz, 2C), 81.6 (s, 5C), 77.4 (d, $^2J_{\text{C-F}} = 21$ Hz, 2C); δ_{F} (Acetone-D₆): -72.67 (d, $^1J_{\text{P-F}} = 707$ Hz), -141.77 (s, 1F); m/z (HR-ESI⁺) 256.9836 [M-PF₆]⁺ (C₁₁H₁₀F⁹⁶Ru requires 256.9842); Anal. Found (Expected): C 32.56 (32.44); H 2.52 (2.48); N 0.25 (0.00).

[CpRu(η^6 -*o*-chlorotoluene)]PF₆

Following the *General Procedure*, [CpRu(NCMe)₃]PF₆ (150 mg, 0.345 mmol) and *ortho*-chlorotoluene (48 mg, 45 μ L, 0.380 mmol, 1.1 equiv) were reacted to produce the *title compound* as a beige solid (147 mg, 97%); δ_{H} (Acetone-D₆): 6.80 (d, $J = 6.0$ Hz, 1H), 6.60 (d, $J = 6.0$ Hz, 1H), 6.39 (td, $J = 6.0, 1.0$ Hz, 1H), 6.31 (t, $J = 6.0$ Hz, 1H), 5.59 (s, 5H, Cp), 2.60 (s, 3H); δ_{C} (Acetone-D₆): 106.7 (s, 1C), 102.3 (s, 1C), 87.5 (s, 1C), 87.3 (s, 1C), 85.3 (s, 1C), 85.2 (s, 1C) 82.5 (s, 5C), 18.6 (s, 1C); m/z (HR-ESI⁺) 286.9703 [M-PF₆]⁺ (C₁₂H₁₂Cl⁹⁶Ru requires 286.9704). Anal. Found (Expected): C 31.69 (31.52); H 2.21 (2.20); N 0.26 (0.00).

[CpRu(η^6 -nitrobenzene)]PF₆

Following the *General Procedure*, [CpRu(NCMe)₃]PF₆ (200 mg, 0.461 mmol) and nitrobenzene (63 mg, 53 μ L, 0.507 mmol, 1.1 equiv) were reacted to produce the *title compound* as a beige solid (187 mg, 93%); δ_{H} (Acetone-D₆): 7.46 (dt, $^3J_{\text{H-H}} = 6.0$ Hz, $^4J_{\text{H-H}} = 2.0$ Hz, 2H), 6.79 (tt, $^3J_{\text{H-H}} = 6.0$ Hz, $^4J_{\text{H-H}} = 2.0$ Hz, 2H), 6.70 (tt, $^3J_{\text{H-H}} = 6.0$ Hz, $^4J_{\text{H-H}} = 2.0$ Hz, 1H) 5.78 (s, 5H); δ_{C} (Acetone-D₆): 111.4 (s, 1C), 88.5 (s, 1C), 86.5 (s, 2C), 83.7 (s, 5C), 82.9 (s, 2C); m/z (HR-ESI⁺) 283.9788 [M-PF₆]⁺ (C₁₁H₁₀NO₂⁹⁶Ru requires 283.9787); Anal. Found (Expected): C 30.47 (30.43); H 2.34 (2.32); N 3.37 (3.23).

[CpRu(η^6 - $\alpha\alpha\alpha$ -trifluorotoluene)]PF₆

Following the *General Procedure*, [CpRu(NCMe)₃]PF₆ (200 mg, 0.461 mmol) and $\alpha\alpha\alpha$ -trifluorotoluene (74 mg, 62 μ L, 0.507 mmol, 1.1 equiv) were reacted to produce the *title compound* as a beige solid (179 mg, 85%); δ_{H} (acetone-D₆) 6.86 – 6.82 (m, 2H), 6.64 – 6.61 (m, 3H), 5.70 (s, 5H); δ_{C} (acetone-D₆)

123.2 (q, $^1J_{C-F}$ 274 Hz, 1C), 91.8 (q, $^2J_{C-F}$ 38 Hz, 1C), 87.8 (s, 1C), 86.2 (s, 2C), 83.6 (q, $^3J_{C-F}$ 3 Hz, 2C), 82.6 (s, 5C); δ_F (acetone- D_6) -62.33 (s, 3F), -72.6 (d, $^1J_{F-P}$ 707 Hz); m/z (HR-ESI $^+$) 306.9812 [M-PF $_6$] $^+$ (C $_{12}$ H $_{10}$ F $_3$ 96 Ru requires 306.9811). Anal. Found (Expected): C 31.69 (31.52); H 2.21 (2.20); N 0.26 (0.00).

[CpRu(η^6 -benzene)]PF $_6$

The reaction is a modification of the existing literature procedure.¹ A 100 mL oven dried round-bottom flask equipped with a stir-bar was charged with finely ground potassium carbonate (0.83 g, 6.00 mmol, 6.0 equiv) and the flask flame-dried under vacuum. After cooling to room temperature, the flask was further charged with [(C $_6$ H $_6$)RuCl $_2$] $_2$ (0.50 g, 1.00 mmol) and a reflux condenser added. Ethanol (30 mL) was then added, followed by freshly cracked cyclopentadiene (1.5 mL, 18.0 mmol, 18 equiv). The resulting heterogeneous brown mixture was then warmed to 85 °C with rapid stirring. After approximately 16 h, the reaction mixture was cooled to room temperature and filtered through a plug of Celite, and the Celite rinsed with a further 25 mL of ethanol. The dark yellow filtrate was concentrated to 20 mL, then an aqueous solution of NH $_4$ PF $_6$ (0.68 g, 4.20 mmol, 4.2 equiv, in 10 mL of H $_2$ O) was added, resulting in the immediate formation of a tan precipitate. The remaining ethanol was removed under reduced pressure and the resulting suspension cooled for several hours. The mixture was then filtered and the tan solid dried under vacuum. The crude product was subsequently dissolved in a minimum of acetonitrile and diethyl ether added dropwise until precipitate formation was no longer observed. This mixture was cooled for several hours before being filtered to give the *title compound* as a light brown solid 0.718 g (92%). The product is spectroscopically identical to the known [(η^6 -C $_6$ H $_6$)Ru(C $_5$ H $_5$)]PF $_6$ ² and is pure by 1 H NMR spectroscopy to the limits of detection. δ_H (acetone- D_6) 6.36 (6H, s, H 1), 5.56 (5H, s, H 2).

Optimization of C-H functionalization

General Procedure for Catalysis

All catalysis runs were performed at high temperature in a sealed Young's Tap flask. The flask was placed in a carousel with a heating block at the bottom and a cooling block at the top.

Solid reagents were weighed out and transferred to an oven dried Young's Tap flask. This was placed under an inert atmosphere, after which the dry and deoxygenated solvent (1 mL) was added via degassed syringe. The liquid reagents were then added via Gilson pipette under a steady stream of argon and then the reaction vessel sealed. The temperature was increased (usually to 120 °C) and the reaction was left for 18 hours.

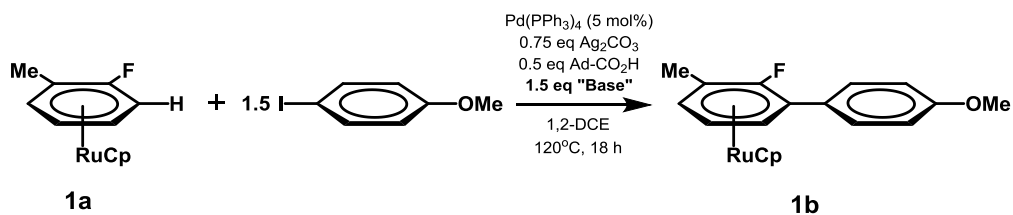
In the case of low boiling point solvents: The volatiles were removed via distillation, replaced with deuterated solvent, sonicated to ensure all dissolvable material was in solution, and then filtered through clean tissue into an NMR tube.

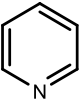
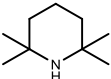
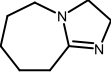

In the case of high boiling point solvents: An aliquot (0.1 mL) of the reaction solution was dissolved in deuterated solvent (0.5 mL) and added directly into an NMR tube.

In both cases, percentage conversion was determined through ratio of all discernible products in the corresponding spectra against internal standards.

Base Screen

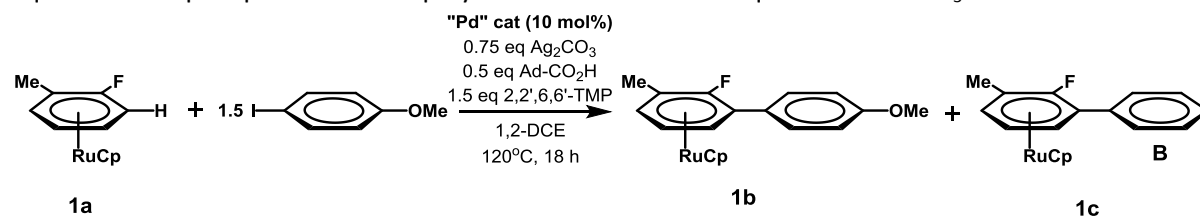
Table S1: Formation of **1b** with variation of organic bases. ^aPercentage of phenylated by-product **1c** (see full text).



Entry	Base	Conversion to 1b (%)
1		7 (Competition with formation of $[\text{Cl}_2\text{Ru(Py)}_4]$)
2		44 (27) ^a
3		0
4		0

Pd Catalyst and Ligand Screen

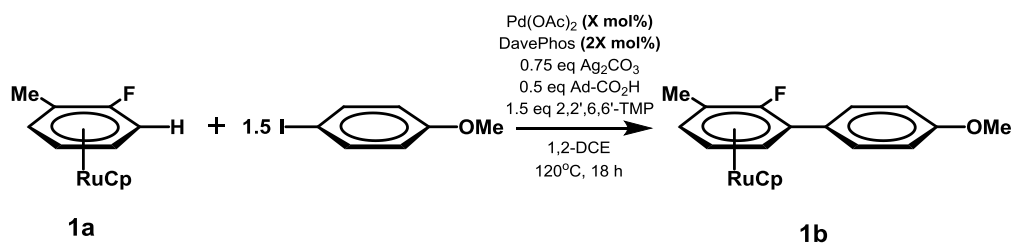
Table S2: Variation of the Pd-based catalyst, 10 mol% of “Pd” was employed in all cases. ^a2 equivalents of phosphine were employed relative to “Pd” ^b3 equivalents of PPh₃ relative to “Pd”



Entry	“Pd” (10 mol%)	Additional Phosphine ^a	Conversion 1b (%)	Conversion 1c (%)
1	Pd(OAc) ₂	^b PPh ₃	41	10
2	Pd(OAc) ₂	-	16	-
3	Pd(OAc) ₂	dppe	51	-
4	Pd(OAc)₂	DavePhos	69	-
5	Pd(OAc) ₂	XantPhos	64	9
6	Pd(OAc) ₂	(R)-Binap	22	2
7	Pd(OAc) ₂	SPhos	49	-
8	PdCl ₂	-	30	-
9	PdCl ₂	dppe	51	-
10	Pd ₂ dba ₃	-	10	-
11	Pd ₂ dba ₃	dppe	34	4
12	Pd ₂ dba ₃	XantPhos	44	18
13	Pd ₂ dba ₃	DavePhos	28	-

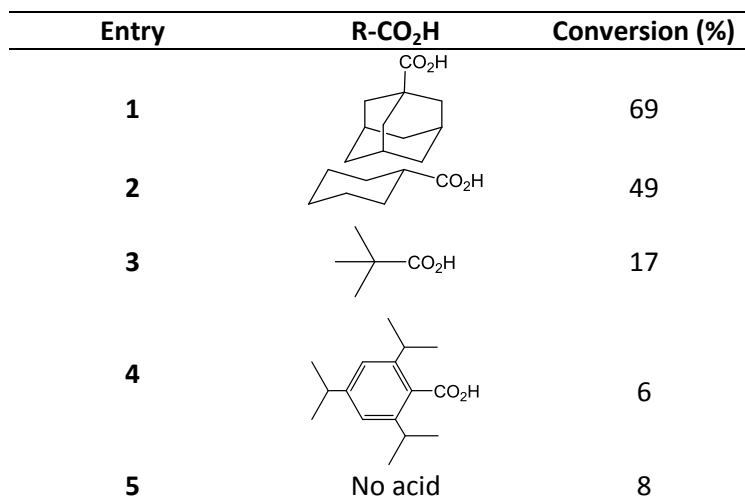
Pd(OAc)₂ Catalyst Loading Screen

Table S3: Variation in mol% of Pd(OAc)₂, two equivalents of DavePhos were employed in each case. ^aformation of disubstituted product.



Entry	Pd(OAc) ₂ (mol%)	Conversion (%)
1	5	50
2	10	69
3	20	75 (5) ^a

Table S4: Variation of carboxylic acid



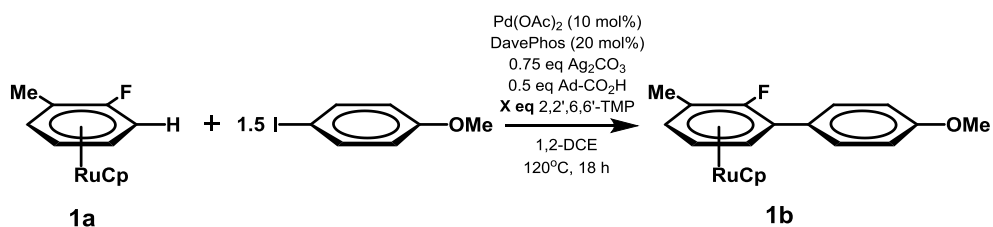
Pd(OAc)₂ (10 mol%)
 DavePhos (20 mol%)
 0.75 eq Ag₂CO₃
 X eq Ad-CO₂H
 1.5 eq 2,2',6,6'-TMP
 1,2-DCE
 120°C, 18 h

1a + 1.5 I-C₆H₄-OMe → **1b**

Entry	Ad-CO ₂ H equivalents	Conversion (%)
1	0.25	31
2	0.50	69
3	0.75	21
4	1.00	21

Base Quantity Screen

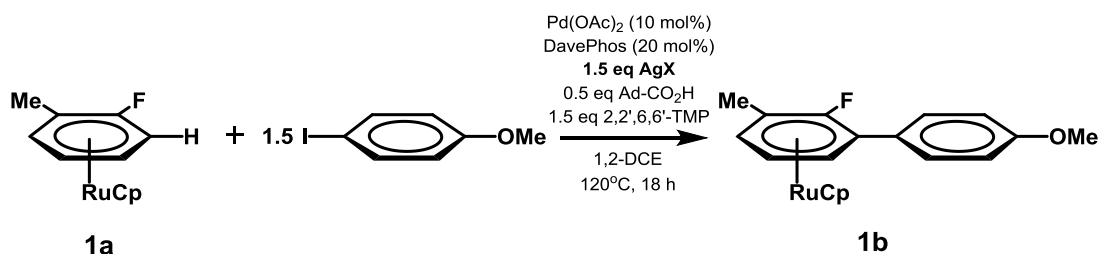
Table S6: Variation of base quantity.



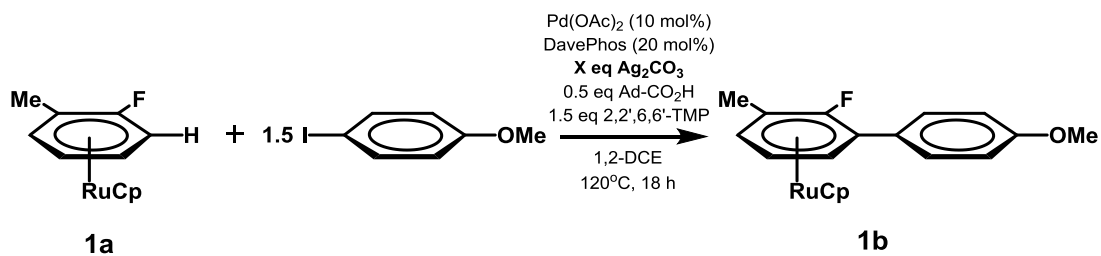
Entry	TMP equivalents	Conversion (%)
1	1	52
2	1.5	69
3	2	57
4	5	53

Silver Screen

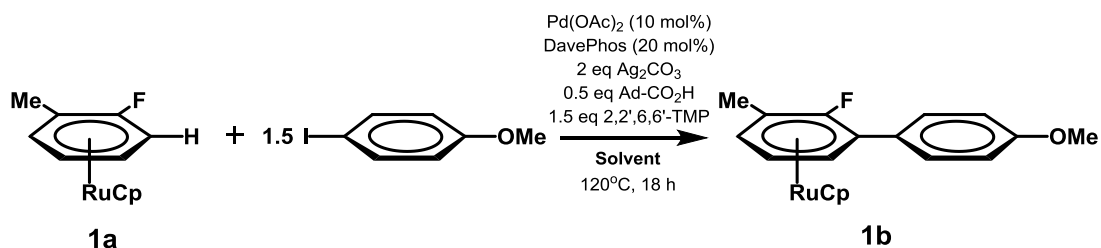
Table S7: Variation of silver salt. 1.5 equivalents of “silver ions” were employed in each case, such that half a molar equivalent of Ag₂CO₃ and Ag₂O were used with respect to other AgX salts.



Entry	“Ag” (1.5 eq.)	Conversion A (%)
1	Ag(O ₂ CCF ₃)	8
2	Ag(OSO ₂ CF ₃)	2
3	Ag(OAc)	11
4	AgPF ₆	0
5	AgNO ₃	22
6	Ag ₂ O	22
7	Ag ₂ CO ₃	69
8	No Ag	0

Table S8: Variation of Ag₂CO₃ quantity.

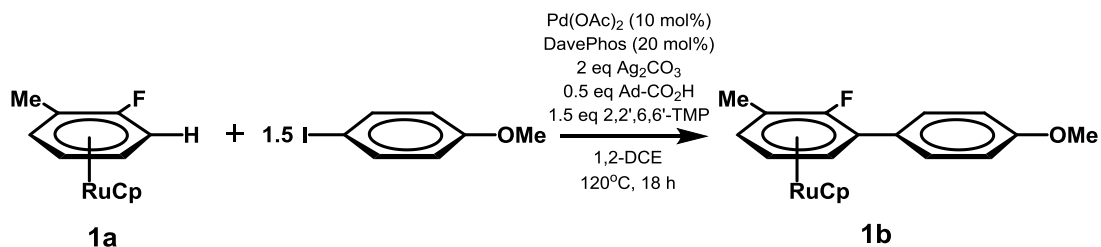
Entry	Ag ₂ CO ₃ (equiv)	Conversion A (%)
1	0	0
2	0.50	29
3	0.75	69
4	1	74
5	2	83

Solvent Screen**Table S9:** Variation of solvent, 1 mL was used in each case.

Entry	Solvent	Dielectric Constant (ε)	Dipole Moment (D)	Conversion (%)
1	1,2-dichloroethane	10.36	1.83	83
2	CHCl ₃	4.81	1.15	23
3	1,4-dioxane	2.25	0.45	46
4	DMA	37.78	3.72	0
5	DMF	36.71	3.86	0
6	MeOH	32.70	2.87	0
7	1-octanol	10.30	1.68	0
8	Cyclohexanone	18.20	3.06	0
9	ⁿ Bu ₂ O	3.10	1.18	0
10	Toluene	2.38	0.31	0

Control Reactions Based on Optimized Reaction Conditions

Table S10: A series of controls were undertaken to establish the necessity of each component to the reaction. oFT = *ortho*-fluorotoluene, Ar-H = **1a**, Ar-I = 4-iodoanisole, Base = 2,2',6,6'-tetramethylpiperidine.



Entry	Ar-H	Ar-I	Pd(OAc) ₂	DavePhos	Ad-CO ₂ H	Base	Ag ₂ CO ₃	Solvent	Conv. (%)
1	✓	✓	✓	✓	✓	✓	✓	1,2-DCE	83
2	✓	X	✓	✓	✓	✓	✓	1,2-DCE	0
3	✓	✓	X	✓	✓	✓	✓	1,2-DCE	0
4	✓	✓	✓	X	✓	✓	✓	1,2-DCE	0
5	✓	✓	✓	✓	X	✓	✓	1,2-DCE	8
6	✓	✓	✓	✓	✓	X	✓	1,2-DCE	59
7	✓	✓	✓	✓	✓	✓	X	1,2-DCE	0

Regeneration of activating Ru complex – Photolysis

A quartz, Young's tap NMR tube was charged with a d_3 -MeCN solution of $[\text{CpRu}(\text{C}_6\text{H}_3\text{MeF}-\text{C}_6\text{H}_4\text{OMe})]\text{PF}_6$ (**1b**). The tube was placed under an ultraviolet lamp (365 nm, 9 W) for a set period of time and ^1H NMR spectra were obtained to determine the extent of photolysis (^1H NMR, d_3 -MeCN, 400 MHz, 298 K).

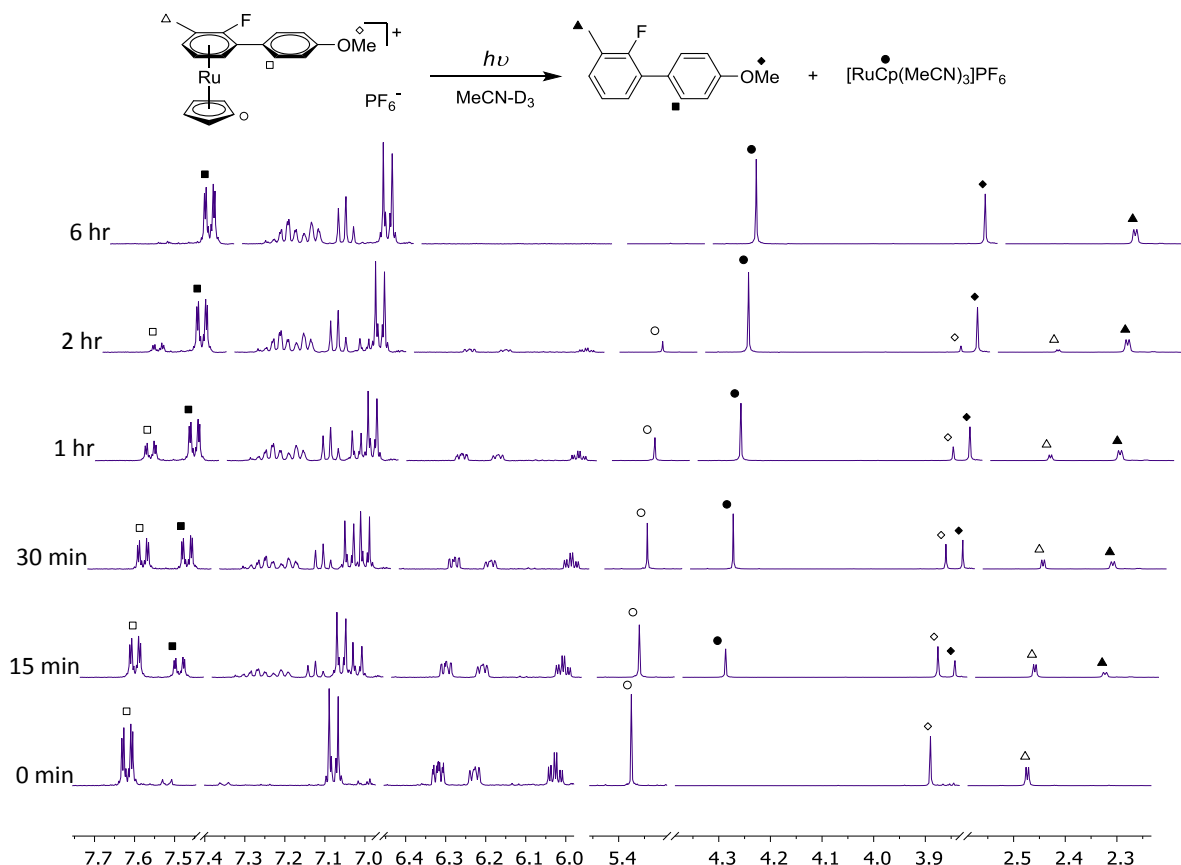


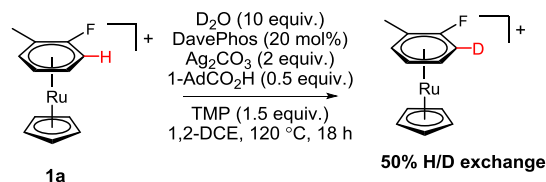
Figure S1. Photolysis (365 nm, 9 W, d_3 -MeCN) over 6 h showing full conversion to the free arene **1d** and $[\text{CpRu}(d_3\text{-NCMe})_3]^+$.

Mechanistic Study

Deuterium Exchange experiment

Complex **1a** was allowed to react under the optimized conditions with 10 equivalents of D_2O in the absence of palladium metal. After 18 hours of reaction, the volatiles were removed via distillation, replaced with deuterated solvent, sonicated to ensure all dissolvable material was in solution, and then filtered through clean tissue into an NMR tube. ^1H - and ^{19}F -NMR were used to analyse the extent of H/D exchange (Figures S2 and S3, respectively). As seen in Figure S2, the relative intensity

of proton **a** decreased, following the exchange reaction, indicating ~50% H/D exchange has taken place. Furthermore, the splitting pattern of proton **b** is significantly altered, due to the presence of the adjacent deuterium ($I = 1$). In the ^{19}F -NMR spectrum, a new peak arises after 18 h, corresponding to the H/D exchange product in 50% conversion (Figure S3). As discussed in the main text, overall, these data show that Ag is likely involved in the key C–H activation mechanistic step.



Scheme S1 NMR experiment to determine C-H activation process.

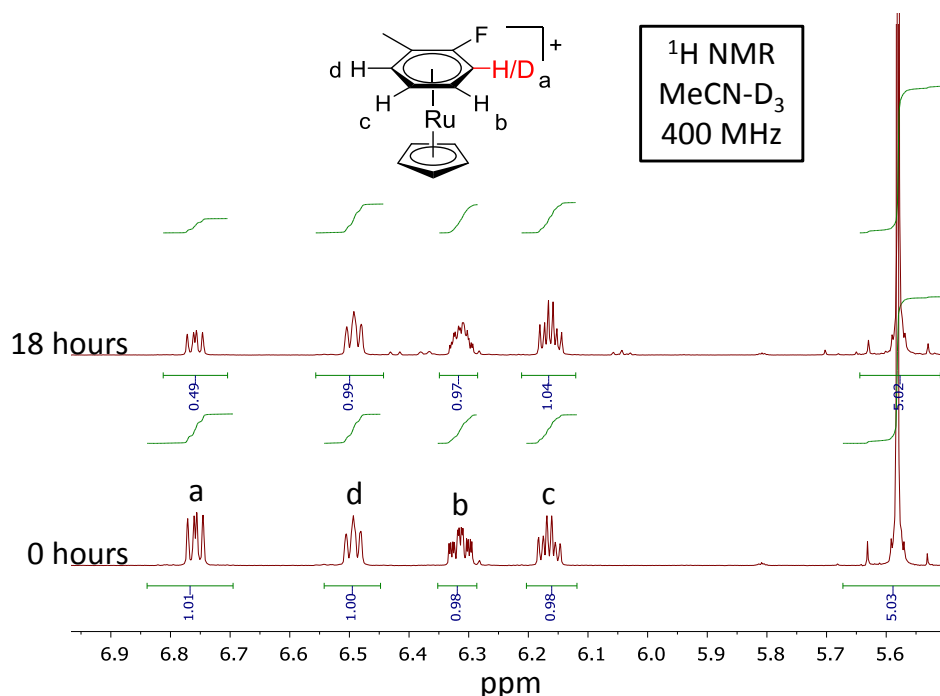


Figure S2. H/D exchange experiment. Analysis by ^1H NMR (NCCD_3 , 400 MHz, 298 K).

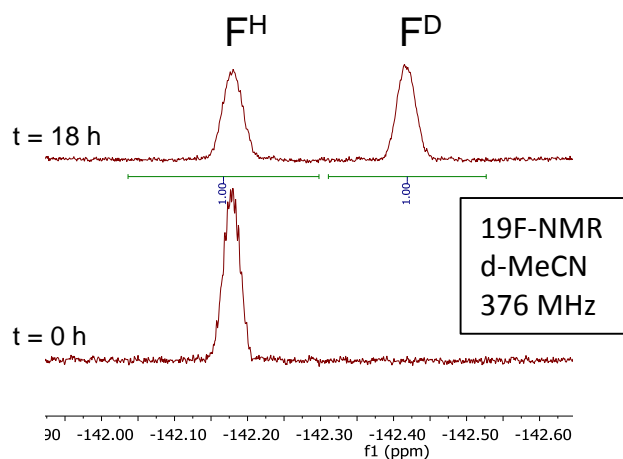
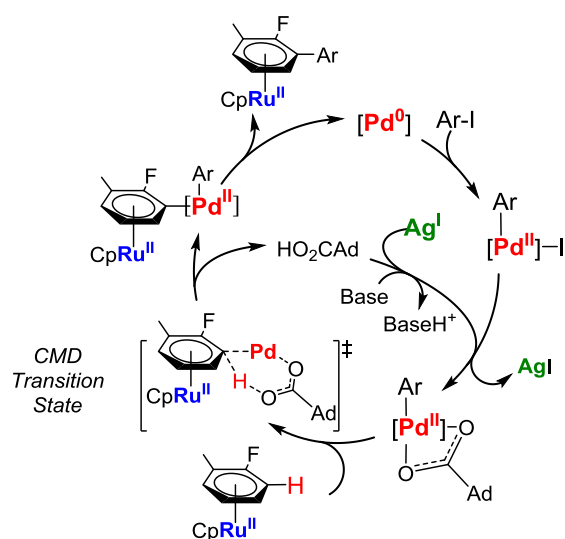


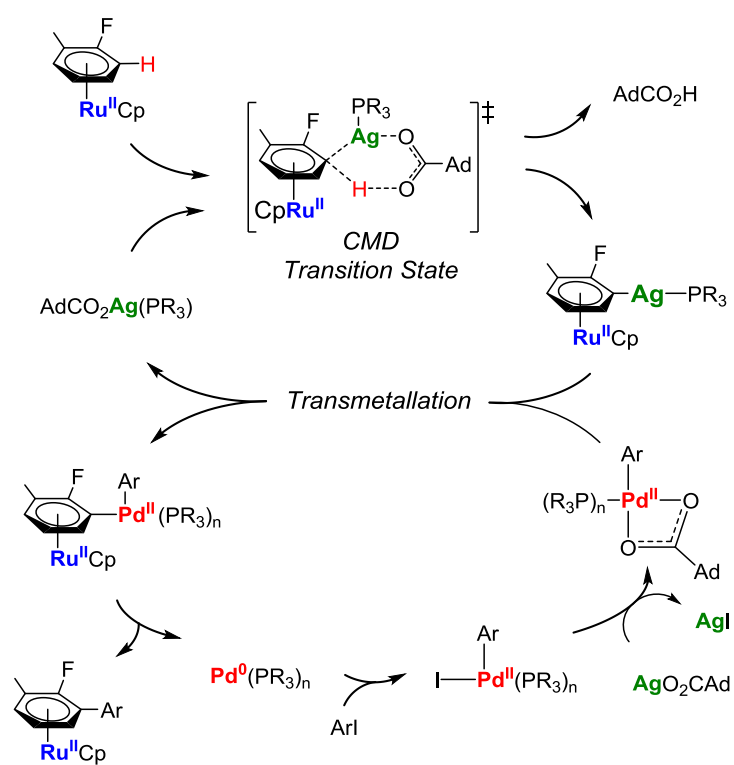
Figure S3. H/D exchange experiment. Analysis by ^{19}F -NMR (NCCD_3 , 400 MHz, 298 K).

Potential Reaction Mechanisms

Scheme S2 presents the concerted metalation-deprotonation mechanism proposed by Fagnou and others,¹ in which Pd is involved in the key C–H activation step. Scheme S3 presents an alternative silver-catalysed C–H activation step, initially proposed by Larrosa² and Sanford.³ Our mechanistic study lead us to conclude that the reaction presented herein proceeds via the Ag-catalysed route, shown in Scheme S3.



Scheme S2. Proposed CMD mechanism, via Pd mediated C–H activation



Scheme S3. Proposed CMD mechanism, via Ag^+ mediated C–H activation

NMR Spectra

[CpRu(η^6 -*ortho*-fluorotoluene)]PF₆

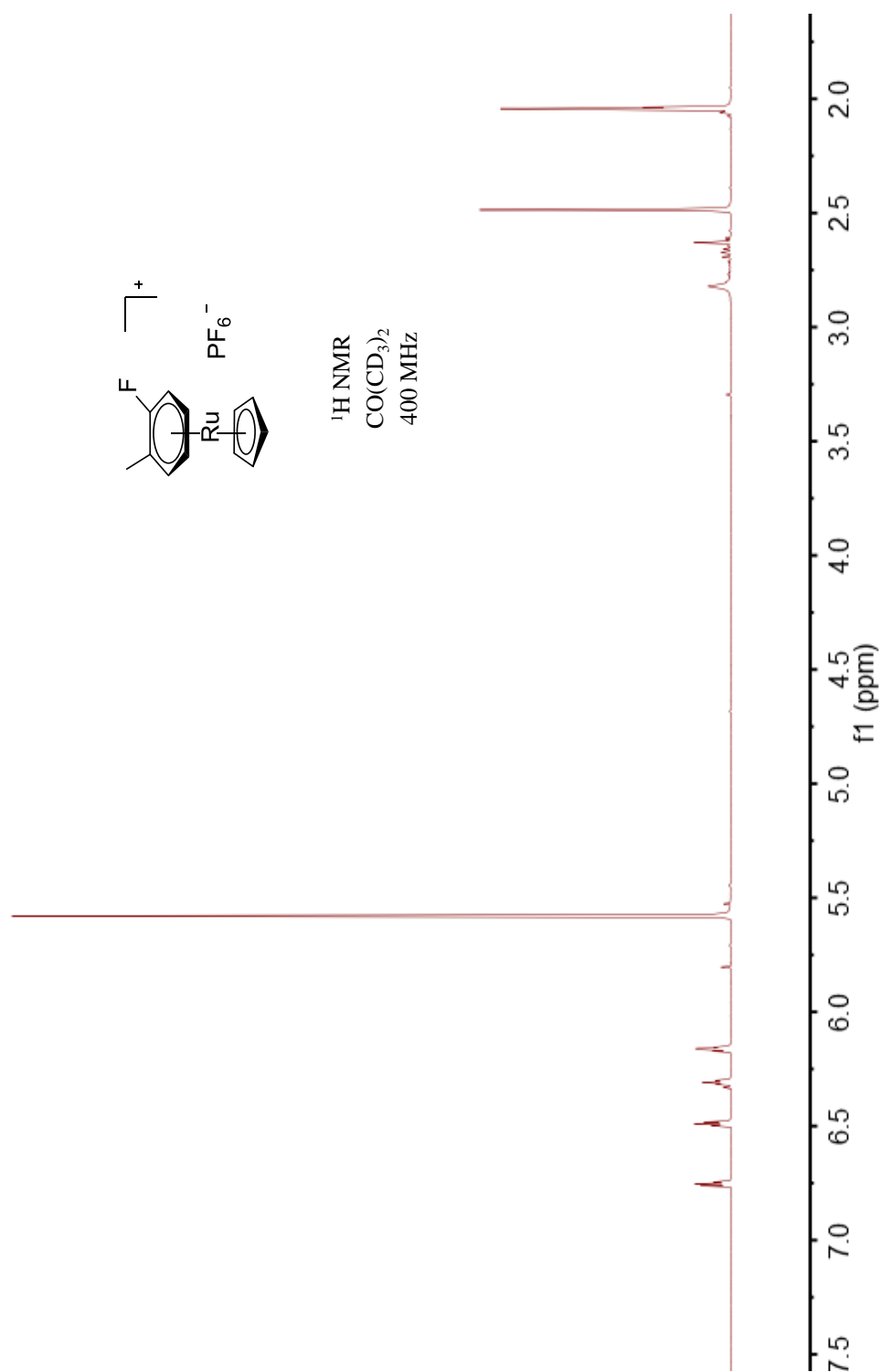


Figure S4 NMR spectrum of compound Table 3, Entry 1, starting complex (¹H-NMR, CO(CD₃)₂, 400 MHz, 298 K)

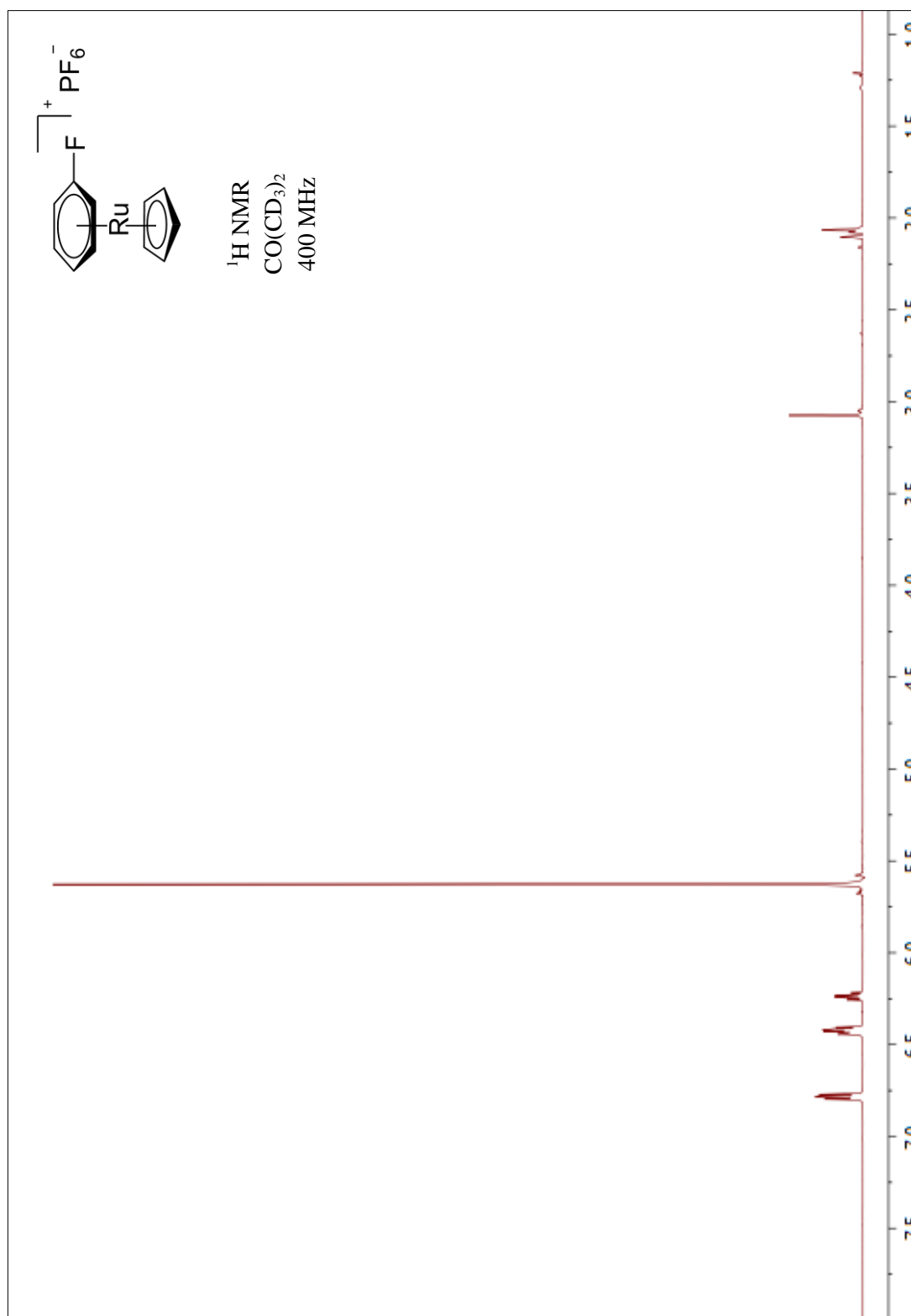


Figure S5 NMR spectrum of compound Table 3, Entry 9, starting complex(¹H-NMR, CO(CD₃)₂, 400 MHz, 298 K)

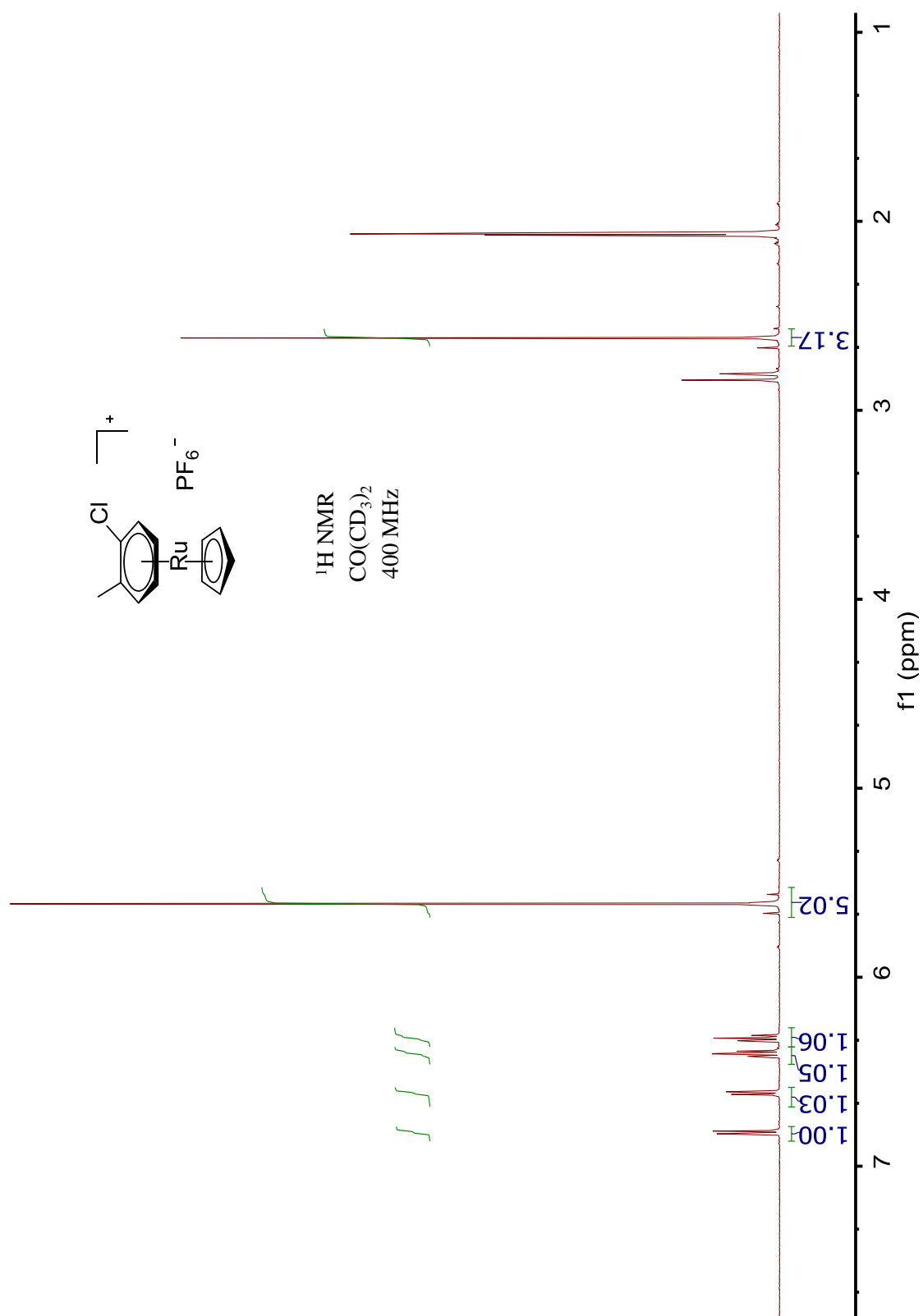


Figure S6 NMR spectrum of compound Table 3, Entry 12, starting complex (^1H -NMR, $\text{CO}(\text{CD}_3)_2$, 400 MHz, 298 K)

[CpRu(η^6 -nitrobenzene)]PF₆

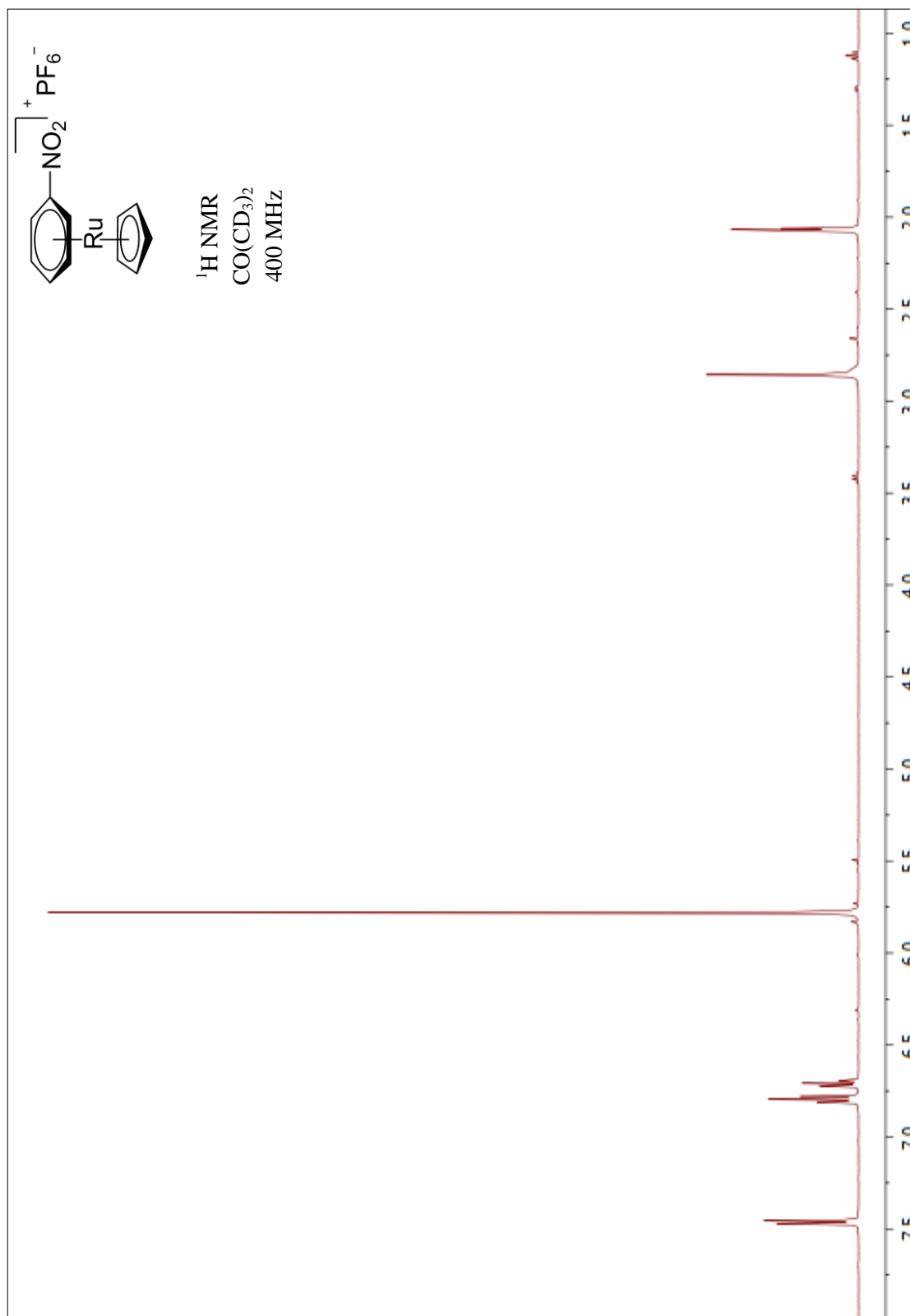


Figure S7 NMR spectrum of compound Table 3, Entry 10, starting complex (¹H-NMR, CO(CD₃)₂, 400 MHz, 298 K)

[CpRu(η^6 - $\alpha\alpha\alpha$ -trifluorotoluene)]PF₆

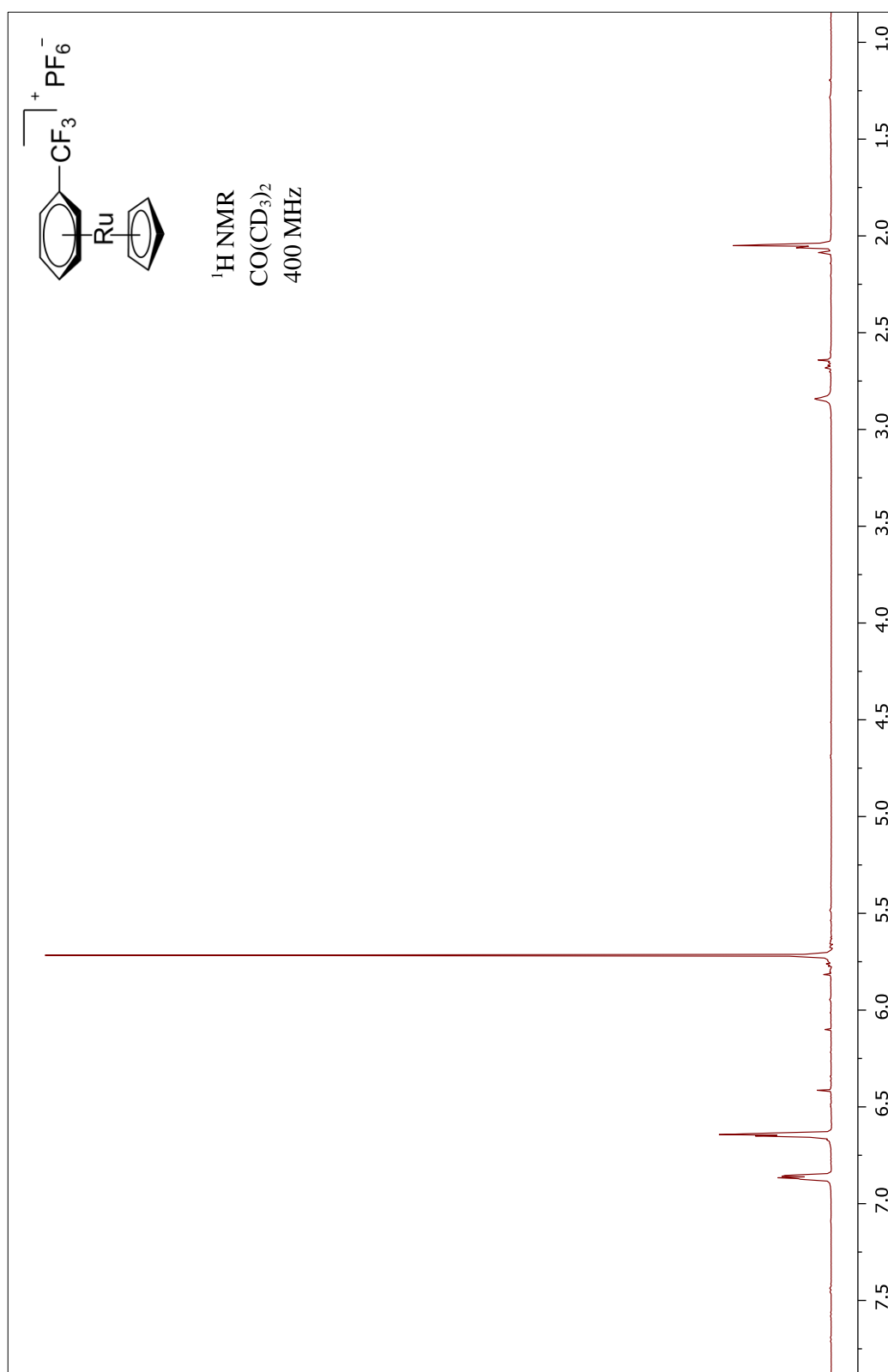


Figure S8 NMR spectrum of compound Table 3, Entry 11, starting complex (¹H-NMR, CO(CD₃)₂, 400 MHz, 298 K)

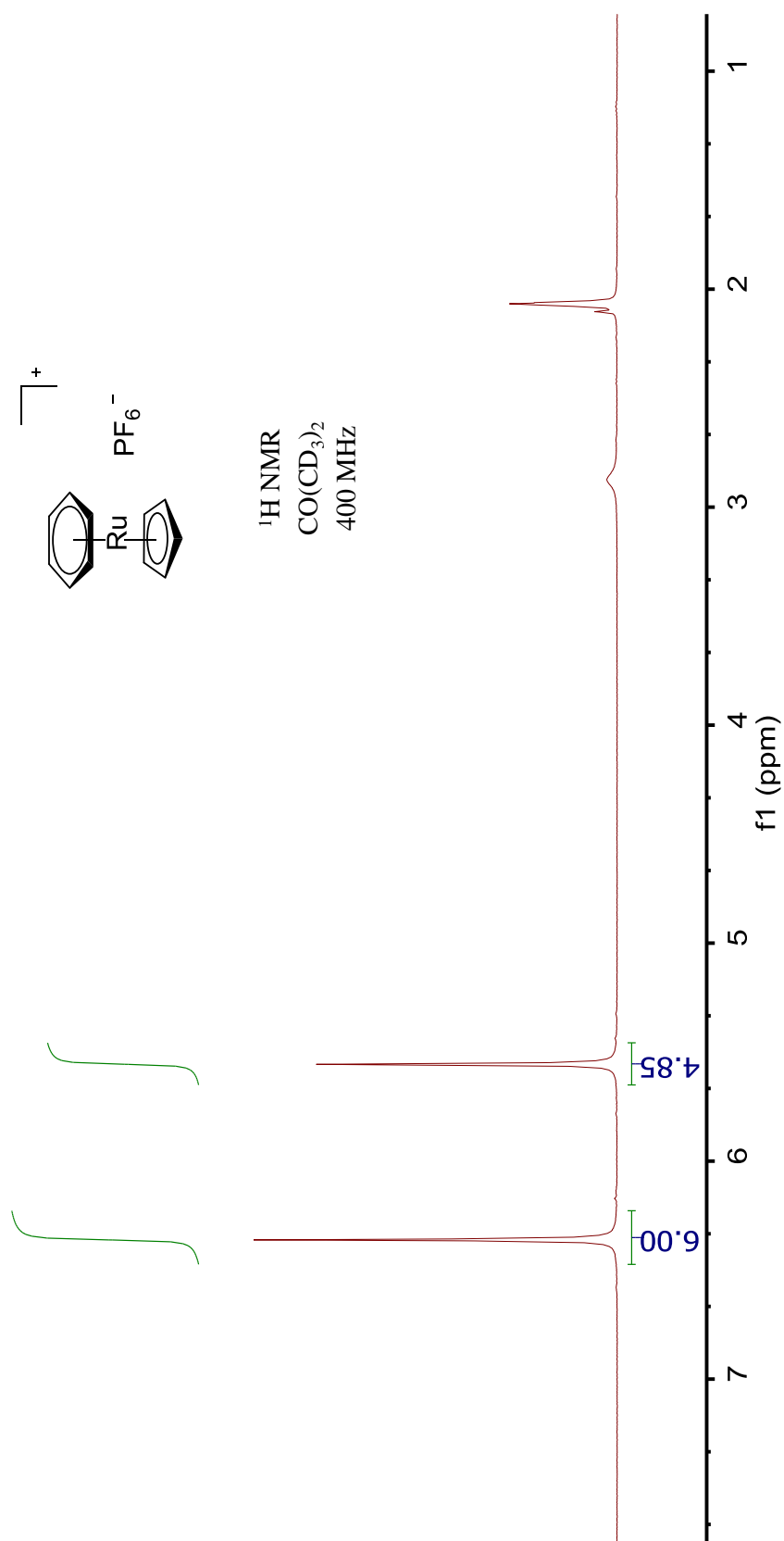


Figure S9 NMR spectrum of compound Table 3, Entry 13, starting complex (^1H -NMR, $\text{CO}(\text{CD}_3)_2$, 400 MHz, 298 K)

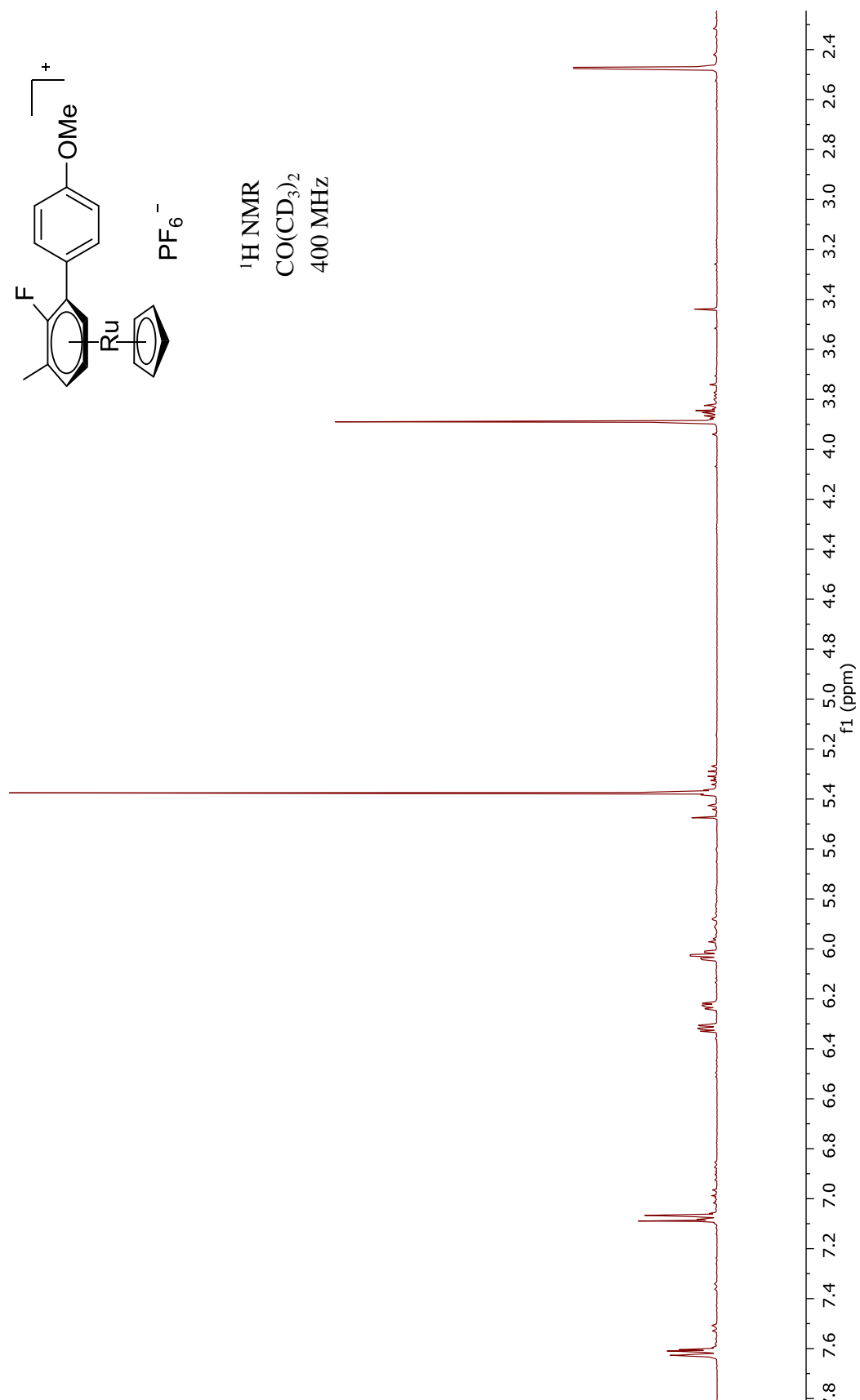


Figure S10 NMR spectrum of compound Table 3, Entry 1, product (¹H-NMR, CO(CD₃)₂, 400 MHz, 298 K)

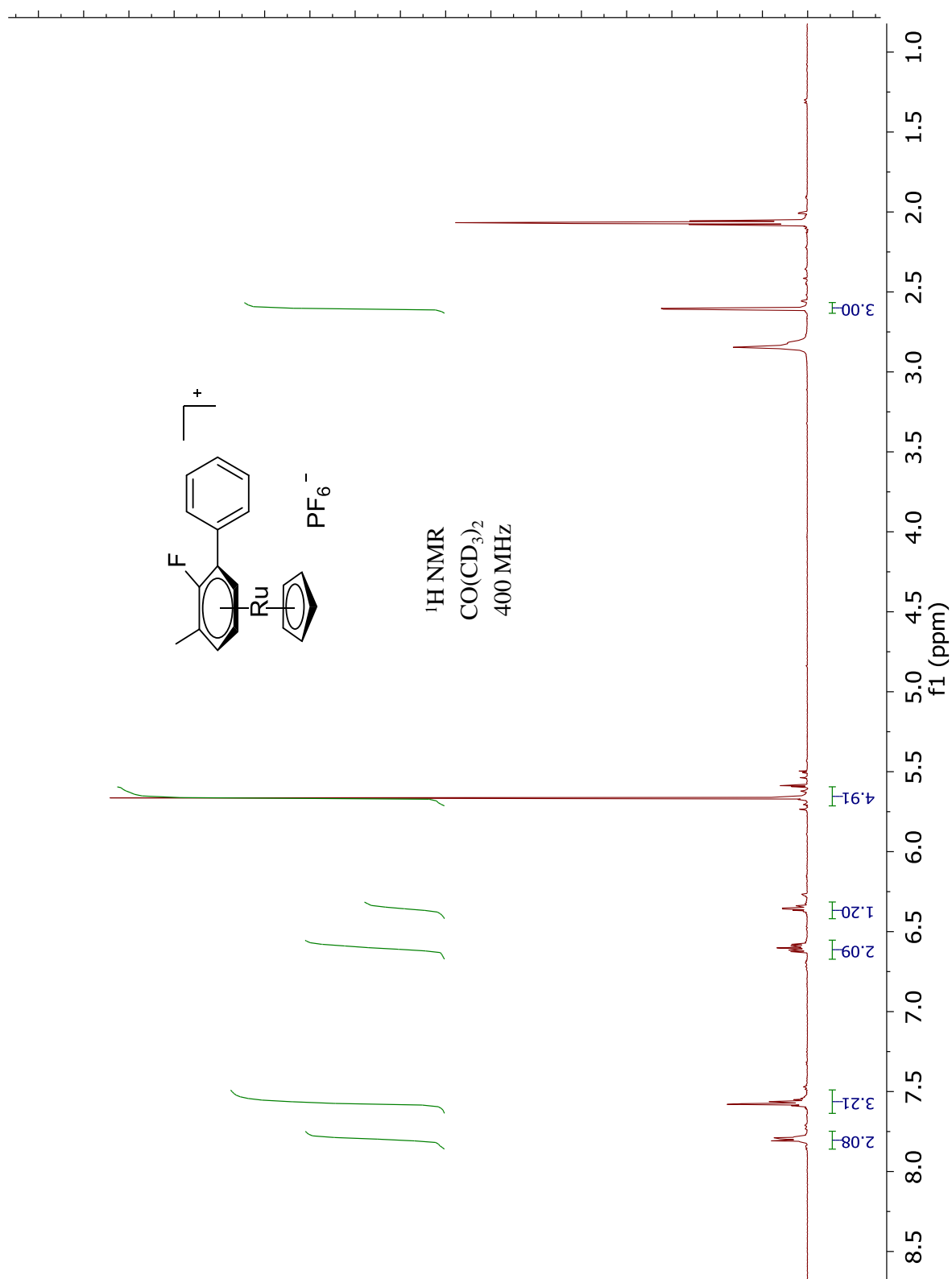


Figure S11 NMR spectrum of compound Table 3, Entry 4, product ($^1\text{H-NMR}$, $\text{CO}(\text{CD}_3)_2$, 400 MHz, 298 K)

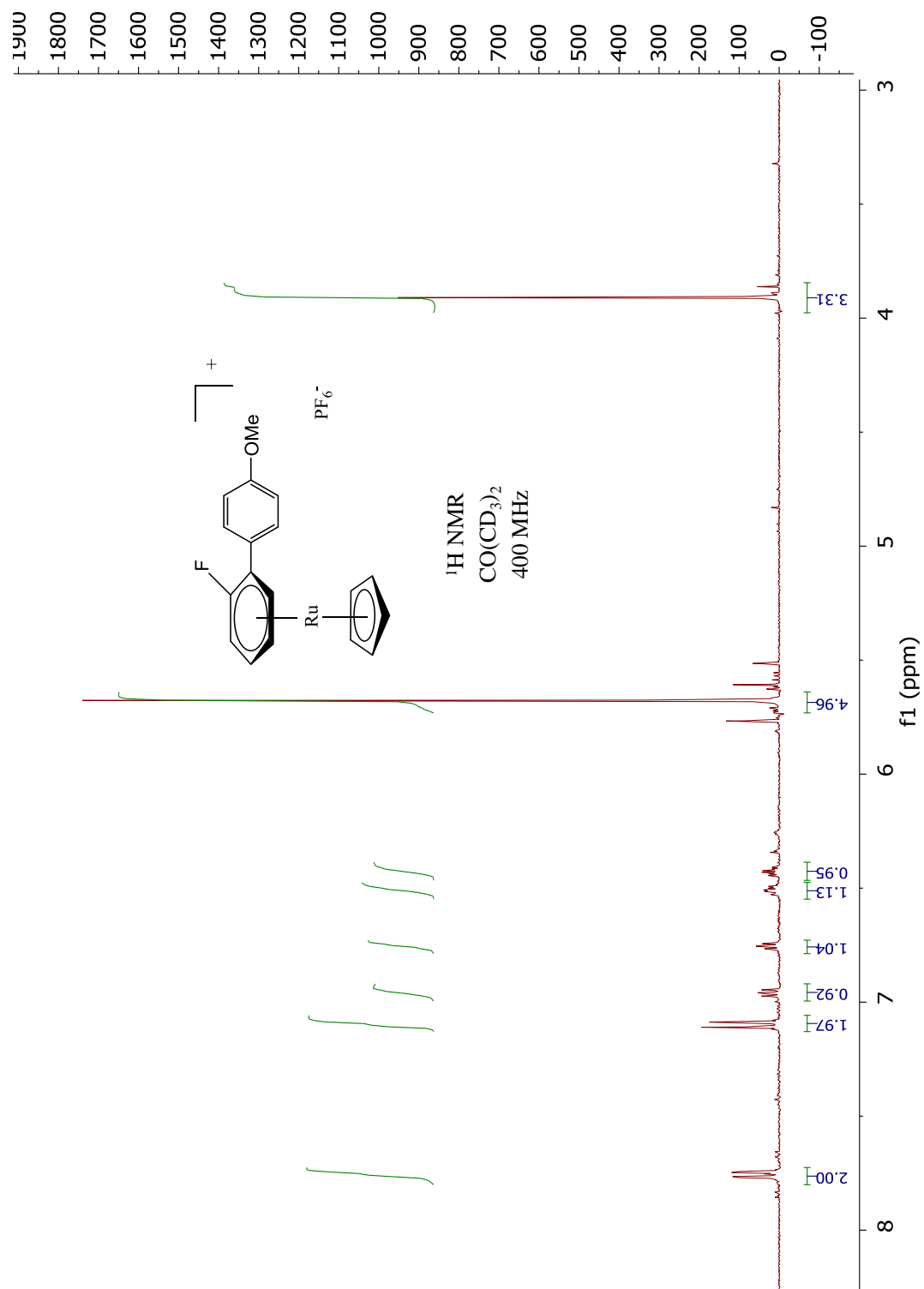


Figure S12 NMR spectrum of compound Table 3, Entry 9, product (¹H-NMR, CO(CD₃)₂, 400 MHz, 298 K)

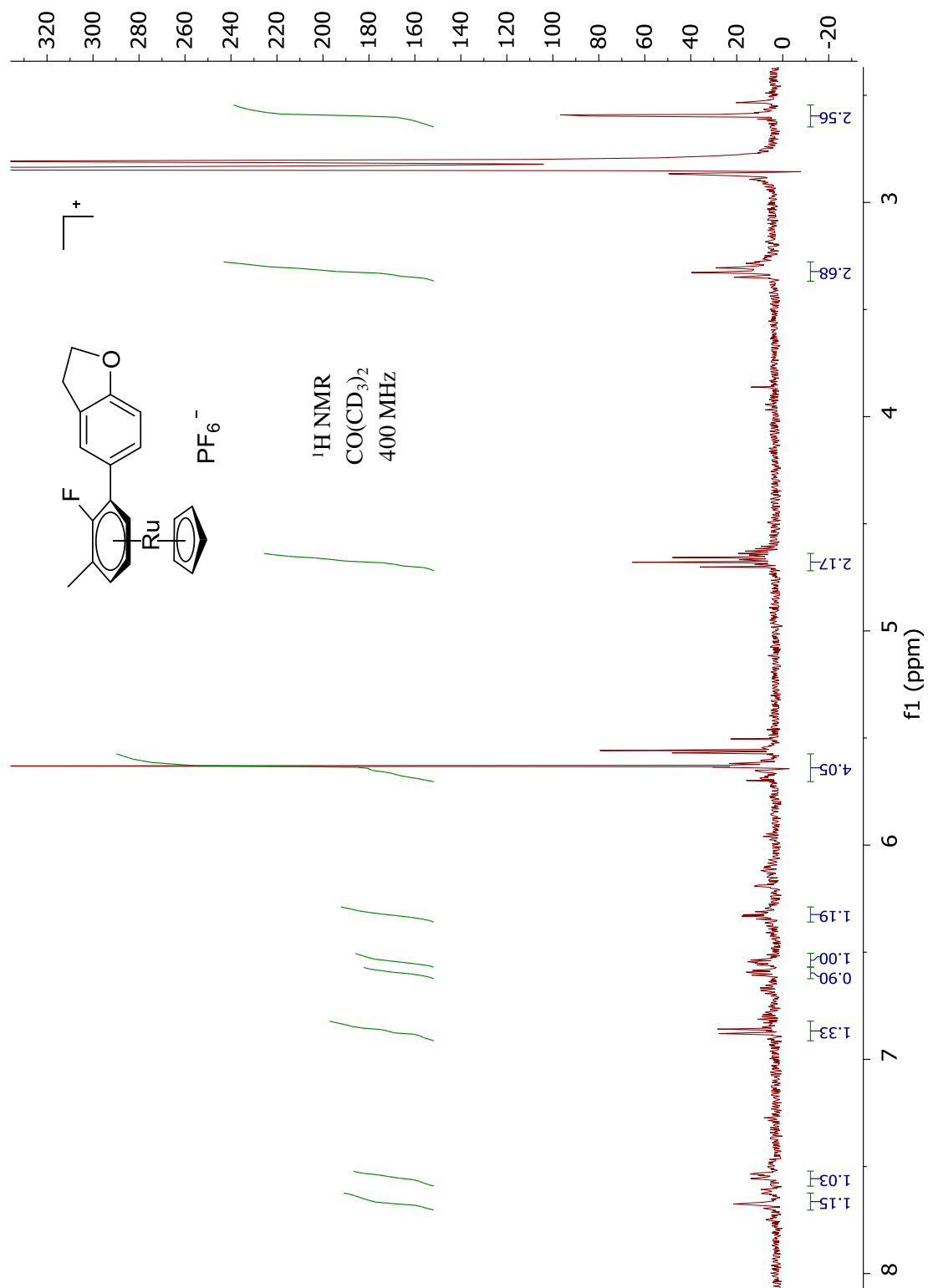


Figure S13 NMR spectrum of compound Table 3, Entry 8, product ($^1\text{H-NMR}$, $\text{CO}(\text{CD}_3)_2$, 400 MHz, 298 K).

References

1. Lafrance, M.; Rowley, C. N.; Woo, T. K.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 8754–8756.
2. Whitaker, D.; Bures, J.; Larrosa, I., *J. Am. Chem. Soc.*, **2016**, *138*, 8384–8387.
3. Lotz, M. D.; Camasso, N. M.; Canty, A. J.; Sanford, M. S., *Organometallics*, **2017**, *36*, 165–171.